Inventors: Maria A. GLUCKSMANN et al.

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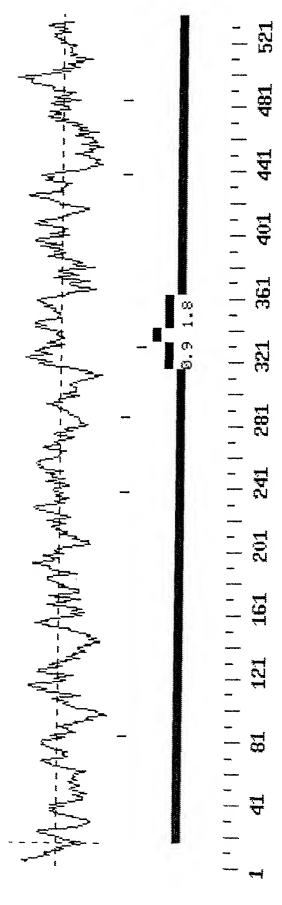
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L Α L Ε · M R Ρ Α P R ATG GCC CTG CTG GCG CGG ATC CTG AGA GCC GGG CTG CGG CCC GAG CGG GCT GGG SEQ ID NO:1 ↑SEQ ID NO:3→ 40 G Ρ R R Ρ Q P R Ρ G L A G Α L CTC CTG GGC GGC GGG GCC CCG CGG CGC CCT CAA CCC GCG GGC GCA CGG CTC CCG GCG GGG 120 G 60 Κ Α G R Р G S Ρ G G G 180 80 E P Α M G P N А R  $\mathbf{T}$ L Α GAG GGT CCC CGG AGC CTC GCC GCC ATG CCG GGG CCG AGG ACC CTC GCC AAC CTG GCG GAG 240 R 100 Ι Η Ε Ι 0 0 TTC TTC TGC AGG GAC GGC TTC AGC CGC ATC CAC GAG ATC CAG CAG AAG CAC ACA CGG GAA 300 Y G K F K S Η F G R 120 P 0 F S TAT GGA AAA ATC TTC AAG TCT CAC TTT GGT CCT CAG TTT GTA GTA TCT ATT GCA GAC CGC 360 V 140 Α R Α Ε E D M L G Α Α М A P Q R GAT ATG GTG GCT CAG GTG CTC CGG GCG GAG GGC GCT GCG CCC CAG AGA GCC AAC ATG GAG 420 Y R D 160 L R G Α E G R Α Т G L I TCC TGG CGG GAG TAC CGA GAC TTG CGG GGG AGA GCC ACC GGG CTC ATC TCG GCG GAG GGT 480 Q W L K M R S V V 180 L R Q R I  $\mathbf{L}$ K Ρ K D GAA CAG TGG CTC AAG ATG AGA AGC GTA TTG AGA CAA AGA ATT CTG AAA CCG AAA GAT GTG 540 G 200 Ε V D Q K Y L Ι I Α D L I R Ι GCC ATT TAT TCT GGA GAA GTC GAC CAA GTT ATT GCT GAC TTA ATT AAA AGA ATC TAC CTC 600 G E V T N N D F 220 CTC AGG AGC CAG GCA GAA GAT GGA GAA ACC GTG ACC AAT GTC AAT GAT CTT TTC TTC AAA 660 G ٧ T I  $\mathbf{L}$ Y G 240 E S R L TAT TCA ATG GAA GGA GTG GCC ACC ATC CTT TAT GAG AGT CGT TTG GGC TGC CTG GAA AAC 720 S 260 Ε Y Ι Ε Α  $\mathbf{L}$ L M M AGC ATC CCA CAG CTG ACT GTG GAA TAC ATC GAG GCC CTG GAG CTC ATG TTT AGC ATG TTC 780 P P 280 K T S Y Α G Α Ι P R F K W R P Ι AAG ACC TCC ATG TAT GCA GGC GCC ATC CCC AGA TGG CTT CGC CCC TTC ATC CCA AAG CCC 840 D 300 R S W D G F S Q Η L K F W 900 TGG CGG GAA TTC TGC AGG TCC TGG GAT GGA CTC TTC AAA TTC AGC CAA ATT CAT GTT GAC G 320 W D Ι Q Y Q М D R G R V S G L K L R N AAC AAG TTG TGG GAC ATA CAG TAC CAA ATG GAC CGA GGC CGG AGG GTG AGC GGG GGA CTT 960 340 F Q T Y L L S Α T Q Ε Α N L L L I Y 1020 CTC ACA TAC CTC TTC CTT AGC CAG GCT CTG ACG CTG CAG GAG ATC TAC GCC AAC GTG ACT 360 M Α G T S F T S W T Y L E L GAG ATG CTG CTG GCC GGC GTC GAC ACG ACG TCC TTC ACC TTG TCT TGG ACG GTG TAC CTC 1080

Title: 27439, NOVEL HUMAN HYDROXYLASE AND USES THEREFOR Inventors: Maria A. GLUCKSMANN et al.
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L CTO		R A AGG	H CAC	P CCA		V GTG							I ATT			N AAT	L TTA	G GGG	380 1140
E GAZ	R AGG	H CAT	V GTT			A GCA	A GCT						L CTG		R AGA	A GCT	L CTC	L CTT	400 1200
K AAG	E GAA	T ACC	L CTG	R AGG	L CTG	F. TTT		L CTG					R CGG	V GTC	T ACC	Q CAG	E GAA	D GAC	420 1260
_	V GTT	I ATT	G GGC	G GGG			I ATT					L CTG		L CTT	C TGC	H CAC	Y TAT	A GCC	440 1320
T ACA		H CAC	Q CAG	D GAT	E GAG		F TTC	R CGG		K AAG	E GAG	F TTC		P CCT	E GAG	R CGC	W TGG	L CTG	460 1380
R CGG		_	D GAC	L TTA	D GAT		V GTT		F TTT		S TCC	I ATC		F TTT	G GGT	H CAT	G GGG	V GTT	480 1440
R CGC	-	_	I ATA		R CGG	R AGA	I ATT	E GAA			I ATT	H CAC		V GTC		I ATC	Q CAG	L TTG	500 1500
L CTT	Q CAA		F TTT				T ACA			T ACC	N AAT	A GCT	V GTT	H CAT	A GCA	K AAA	T ACC	H CAC	520 1560
G GGG	L CTC	L CTG	T ACG	P CCA	G GGG		P CCC	H CAC	V GTG	R CGA	F TTT	V GTT	N AAC	AGA	K AAG QIDN	TAA			538 1614
			AACC CGAT																
TGCAAAGTAATGTAAAAAGGTTGCTATTTTACTGGTGCATACCAGAAGTTGCCCTTTCTTT																			
AAAACCAGTGGCAGTGAATTTTTATGCTTCATACATTGNGCTAGACTCAATATTTAATGACTGGCAGTATCCTGTGCAT TTACTTGTACAGGGAAATGGTGGNTTACTTACAAATTCAGTTCTTC																			



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27439	69	*->PPgPpplPliGnll.qlgrapgpiph.sltklrkakrYGkpvftlyl seQ ID NO:4 PgP l ++ ++ g+ i h++ +k + + YG ++f ++ MPGPRTLANLAEFFcRDGFSRI-HeIQQKHTR-E-YG-KIFKSHF 109
27439	110	GprpvVvltgpeavkevLidkgeeFakgRgdfnptfpwlskgyre Gp+ vV + + ++v +vL +g ++ R + + w+ yr+ +++ GPQFVVSIADRDMVAQVLRAEGAAPQRANMESWREYRDlrgra 152
27439	153	qgllfsdnGpkWrklRrFslltlrfHFgmGaysKrsqkleePriqeeard +gl+ + +G++W k+R l +r +++ +++++ d TGLISA-EGEQWLKMRSVLRQRI-LKPKDVAIYSGEVDQVIAD 193
27439	194	Lverlrkeqa.gspi.DitellarlaplnvIcsllFGvrfdylr  L++r+ ++++++++++++++++++++++++++++++++
27439	243	<pre>peDp.eflklidkllnemfdrvspwhqlldifP.fLlrylpgslfrkafk p + e++ +++ l+ mf ++s+ ++ +P++L+++ p++ +r+ + PQLTvEYIEALE-LMFSMF-KTSMYAG-AIPrWLRPFIPKP-WREFC- 285</pre>
27439	286	<pre>aakd.lkdyldklieerretlepagdpRrlD.igflDslLleakr + +d+l+++ + + + + + + + + + ++++++ RSWDgLFKFSQIHVDNKLWDI-QYQMDrGrrvsgGLL-T-YLFLSQ 328</pre>
27439	329	eggnpkselsdeelaatvldllfAGteTTsstLswaLylLakhPevqakl l+ e+ a+v ++l AG++TTs tLsw++ylLa+hPevq+ +ALTLQEIYANVTEMLLAGVDTTSFTLSWTVYLLARHPEVQQTV 371
27439	372	reEideviGrdrsptydvDaraqmPYLdAvIkEtLRlypvvPlllpRvat + Ei +G pt D +++ P++ A +kEtLRl+pv+P + +Rv+ YREIVKNLGERHVPTAA-D-VPKVPLVRALLKETLRLFPVLP-GNGRVTQ 418
27439	419	kDteiPdGylIPKGtlVivnlyslhrDpkvfpnPeeFdPeRFLde +D +i +GylIPKGt+ ++ y+ + ++ fp++ eF+PeR+L++++ d EDLVI-GGYLIPKGTQLALCHYATSHQDENFPRAKEFRPERWLrkgdlDR 467
27439	468	ngkfkksyaflPFGaGpRnClGerlArmElflfLatlLqrFPelelavpp + + +PFG+G+R+C+G+r+A++E+ l++++lLq+F e++++ + VDNFGSIPFGHGVRSCIGRRIAELEIHLVVIQLLQHF-EIKTSSQT 512
27439	513	gdipsltpkpelglpskpplykvqlrpa<-* ++ + + ++l++ +p++ +r + NAVH-AKTHGLLTPGGPIHVR-F 533

FIG. 3

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Query:	146 RDLRGRATGLISAEGEQWLKMRSVLRQRILKPKDVAIYSGEVDQVIADLIKRIYLLRSQA 205 RD RG A GL++AEGE+W ++RS L +++KP++V Y ++++V D ++R+ +R Q
Sbjct:	11 RDYRGEAYGLLTAEGEEWQRLRSALNPKLMKPQEVKNYIPKLNEVSQDFVERLRKMRDQG 70 SEQ ID NO:5
Query:	206 E-DGETVTNVNDLFFKYSMEGVATILYESRLGCLE-NSIPQLTVEYIEALELMFSMFKTS 263 + GE V + + +K++ E + T+L+ RLGCLE N++ ++I+A++ SMF T+
Sbjct:	71 QGQGELVEDFAEELYKWAFESICTVLFGKRLGCLEENNVDPEAQKFIDAVKSMFHTT 127
Query:	264 MYAGAIPRWL-RPFIPKPWREFCRSWDGLFKFSQIHVDNKLWDIQYQMDRG 313 + +P L R F K W++ R+WD +F O ++D L ++ + G
Sbjct:	128 VPMMNMPPELWRYFKTKTWKDHVRAWDQIFDVCQKYIDEALERLEKESQSG 178

# FIG. 4

Query:	71	GPRTLANLAEFFCRDGFSRIHE-IQQKHTREYGKIFKSHFG-PQFVVSIADRDMVAQVLR G + L + G + +H+ I +H ++YG IF+ G Q V ++ +++ V +	128	
Sbjet: NO:6	64	GLPVVGTLVDLIAAGGATHLHKYIDARH-KQYGPIFRERLGGTQDAVFVSSANLMRGVFQ	122	SEQ ID
Query:	129	AEGAAPQRANMESWREYRDLRGRATGLISAEGEQWLKMRSVLRQRILKPKDVAIYS EG PQ ++W Y GL EG +WL R +L + +L DV I S	184	
Sbjct:	123	HEGQYPQHPLPDAWTLYNQQHACQRGLFFMEGAEWLHNRRILNRLLLNGNLNWMDVHIES	182	
Query:	185	GEVDQVIADLIKRIYLLRSQ~-~AEDGET~-VTNVNDLFFKYSMEGVATILY-ESRLG + + D KR + AE GE + + ++++S+E + I++ S L	236	
Sbjct:	183	CTRRMVDQWKRRTAEAAAIPLAESGEIRSYELPLLEQQLYRWSIEVLCCIMFGTSVLT	240	
Query:	237	CLENSIPQLTVEYIEALELMFSMFKTSMYAGAIPRWLRPFIPKP-WREFCRSWDGLFKFS C + Q +++Y +++ +F+ S P L + P WR+F + D + +	295	
Sbjct:	241	CPKIQSSLDYFTQIVHKVFEHSSRLMTFPPRLAQILRLPIWRDFEANVDEVLREG	295	
Query:	296	QIHVDNKLWDIQYQMDRGRRVSGGLLTYLFLSQALTLQEIYANV-TEMLLAGVDTTSFTL +D+ I+ Q D+ R L Y L A ++ + ++++A DTT+F+	354	
Sbjct:	296	AAIIDHCIRVQEDQRRPHDEALYHRLQAADVPGDMIKRIFVDLVIAAGDTTAFSS	350	
Query:	355	SWTVYLLARHPEVQQTVYREIVKNLGERHVPTAADVPKVPLVRALLKETLRLF 407 W ++ L++ P +QQ + +E N R L+ L+KE+LRL+		
Sbjct:	351	QWALFALSKEPRLQQRLAKERATN-DSRLMHGLIKESLRLY 390		

# FIG. 5

Query:	66	LAAMPGPRTLANLAEFFCRDGFSRIHEIQQKHTREYGKIFKSHFGPQFVVSIADRDMVAQ 125
Sbjct:	37	LA +PGP TL L + FC+ +HE+Q YG ++ S FG Q V++A +V Q LADIPGPGTLRFLFQLFCKGYLLHLHELQVLGKARYGPMWMSSFGTQRTVNLASPPLVEQ 96 SEQ ID NO:7
Query:	126	VLRAEGAAPQRANMESWREYRDLRGRA 152
Sbict:	97	V+R EG P R + E W+E+R RA VMRQEGKYPVRCSFEPWKEHRRRHQRA 123

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389 DVPKVPLVRALLKETLRLFPVLPGNGRVTQEDL----VIGG-YLIPKGTQLALCHYATSH 443 Query:

+GG Y IPKGTQ+ + Y +H D+ K+P + A++KETLRL P +P R ++D+

8 DLQKLPYLDAVIKETLRLHPPVPTVMRKVKKDMEVSGTVGGEYTIPKGTQVMVSPYVMTH 67 SEQ ID NO:8 Sbjct:

444 QD-ENFPRAKEFRPERWLRKGD 464 Query:

+D E +P +EF PERWL

68 RDPEYYPDPEEFNPERWLEPSE 89 Sbjct:

#### FIG. 7

99 REYGKIFKSHFGPQFVVSIADRDMVAQV-LRAEGAAPQRANMESWREYRDLRGRATGLIS 157 Query:

L + GL G Q ++ IA+ ++ +V ++ P R+ + S ++YG IF+

74 KQYGPIFRFQMGRQPLIIIAEAELCREVGIKKFKDLPNRS-IPSPISASPLHKK--GLFF 130 SEQ ID Sbjct:

NO:9

158 AEGEQWLKMRSVLRQRILKPKDVAIYSGEVDQVIADLIKRIYLLRSQAEDGETVTNVNDL 217 Query:

++W KMR+ + ++P + + + + + + + L S+ D

131 TRDKRWSKMRNTILS-LYQPSHL---TSLIPTMHSFITSATHNLDSKPRD----IVFSNL 182 Sbjct:

218 FFKYSMEGVATILYESRLGCLENSIPQLTVEYIEAL-ELMFSMFKTSM-YAGAIP---RW 272 Query:

FK+++ + GL P VE ++++S + M +G++

183 FLKLTTDIIGQAAFGVDFG-LSGKKPIKDVEVTDFINQHVYSTTQLKMDLSGSLSIILGL 241 Sbjct:

273 LRPFIPKPWREFCRSWDGLFKF----SQIHVDNKLWDIQYQMDRGRRV-SGGLLTYL--- 324 Query:

L P + +P+R+ + G + + +L+I + +

242 LIPILQEPFRQVLKRIPGTMDWRVEKTNARLSGQLNEIVSKRAKEAETDSKDFLSLILKA 301 Sbjct:

325 ----FLSQALTLQEIYANVTEMLLAGVDTTSFTLSWTVYLLARHPEVQQTVYREIVKNL 379 Query:

T I A E LLAG TT+FTLS +YL++ H +V++ + +EI

302 RESDPFAKNIFTSDYISAVTYEHLLAGSATTAFTLSSVLYLVSGHLDVEKRLLQEI-DGF 360 Sbjct:

380 GERH-VPTAADVP-KVPLVRALLKETLRLFPV 409 Query:

G R +PTA D+ K P + ++KE +R + V

361 GNRDLIPTAHDLQHKFPYLDQVIKEAMRFYMV 392 Sbjct:

#### FIG. 8

68 AMPGPRT---LANLAEFFCRDG-FS--RIHEIQQKHTREYGKIFKSHFGP-QFVVSIADR 120 Query:

PQ+V+D+YG I + G +S R+H+ Q + NL + A+PGPR

23 AIPGPRGPFGMGNLYNYLPGIGSYSWLRLHQAGQDKYEKYGAIVRETIVPGQDIVWLYDP 82 SEQ ID Sbjct:

NO:10

121 DMVAQVLRAEGAAPQRANMESWREYRDLRG---RATGLISAEGEQWLKMRSVLRQRILKP 177 Query:

PQR + + +YR R + TGL+ G + W + + R + + + + + P

83 KDIALLLN-ERDCPQRRSHLALAQYRKSRPDVYKTTGLLPTNGPEWWRIRAQVQKELSAP 141 Sbjct:

Query: 178 KDVAIYSGEVDQVIADLIK 196

K V + +VD V + I+

Sbjct: 142 KSVRNFVRQVDGVTKEFIR 160

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Query:	88	SRIHEIQQKHTREYGKIFKSHFGPQFVVSIADRDMVAQVLRAEGAAPQRANMESWREYRD + ++++ + + E K FG ++ + ++ + +AQ+ + E + N + Y	147	
Sbjct: NO:11	52	TELYDLYIRESMEKYGAVKFFFGSRWNILVSRSEYLAQIFKDEDTFAKSGNQKKI-PYSA	110	SEQ ID
Query:	148	LRGRATGLISAEGEQWLKMRSVLRQRILKPKDVAIYSGEVDQVIADLIKRIYLLRSQA L TG +ISA G W R+ + + D I+ +++ LIK L	205	
Sbjct:	111	LAAY-TGDNVISAYGAVWRNYRNAVTNGLQHFDDAPIFKNAKILCTLIKNRLL	162	
Query:	206	EDGETVTNVNDLFFKYSMEGVATILYESRLGCLENSIPQLTVEYIEALELMFS-MFKTSM +G+T + L + +++ ++ + + + + + + + + + + + +	264	
Sbjct:	163	-EGQTSIPMGPLSQRMALDNISQVALGFDFGALTHEKNAFHEHLIRIKKQIFHPFFLTFP	221	
Query:	265	YAGAIPRWLRPFIPKPWREFCRSWDGLFKFSQIHVDNKLWDIQYQMDRGRRVSGGLLTYL + +P P K +++ + L K Q + N Y+ ++ + L+	324	
Sbjct:	222	FLDVLPIPSRKKAFKDVVSFRELLVKRVQDELVNNYKFEQTTFAASDLIR-A	272	
Query:	325	FLSQALTLQEIYANVTEMLLAGVDTTSFTLSWTVYLLARHPEVQQTVYREIVKNLGERHV ++ + ++ ++ N+ +L+AG + +++YLLA++ Q R+ V ++	384	
Sbjct:	273	HNNEIIDYKQLTDNIVIILVAGHENPQLLFNSSLYLLAKYSNEWQEKLRKEVNGITD	329	
Query:	385	PTAADVPKVPLVRALLKETLRLFPVL 410 P + +PL+ A L E +R++P L		
Sbjct:	330	PKGLADLPLLNAFLFEVVRMYPPL 353		

# FIG. 10

Query:	396	VRALLKETLRLFPVLPGNGRVTQEDLVIGGYLIPKGTQLALCHYATSHQDENFPRAKEFR 455 +R + ET+RL + P R + + + GY IP T + + +
Sbjct: NO:12	23	LRQVQDETIRLSTLAPWAARYSDKKVTVCGYTIPAKTPMIHALGVGLKNKTVWENTDSWD 82 SEQ ID
Query:	456	PERWLRKGDLDRVDNFGSIPFG-HGVRSCIGRRIAELEIHLVVIQLLQHFEIKTSSQTNA 514 P+R+ G R ++F PFG H R C G + E+ + LL FEI
Sbjct:	83	PDRFSPNGRRGNDFCPFGVHSRRKCPGYLFSYFEVGVFASILLSRFEIVPVEGQTV 138
Query:	515	VHAKTHGLLT-PGGPIHVRFVNRK 537 + + HGL+T P I + +RK
Sbict:	139	IOVHGLVTEPKDDIKIYIRSRK 160

# FIG. 11

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Query: 344 LAGVDTTSFTLSWTVYLLARHPEVQQTVYREIVKNLGERHVPTAADVPKVPLVRALLKET 403

+AG+DT + +L++ +Y + H E + E L PTA + + PL+ + ET

247 IAGMDTAANSLAFVLYRMHLHSEFLPALRAE-ADALFRDGPPTAEALGRSPLLHRFVMET 305 SEQ ID

Sbjct: NO:13

Query: 404 LRLFPVLP 411

LR+ P+ P

Sbjct: 306 LRVHPIAP 313

#### FIG. 12a

Query: 69 MPGPRTLANLAEFFCRDGFSRIHEIQQKHTREYGKIFKSHFGPQFVVSIADRDMVAQVLR 128

+P P L + AE G ++ + + YG +F+ Q + +A + ++

Sbjct: 2 VPAPPFLGHAAEM----GTIKLRPFLTRCYQAYGPVFQLTVPGQKITVLAGPEANLFAMK 57 SEQ ID

NO:14

Sbjct:

Query: 129 AEGAAPQRANMESWREYRDLRGRATGLISAEGEQWLKMRSV 169

EG R+ +E+WR+ G +IS +G + R V 58 -EGHRVLRS-LEAWRDNDHEMGSDRSMISLDGAEHRAYRRV 96

### FIG. 12b

Query: 153 TGLISAEGEQWLKMRSVLRQRILKPKDVAIYSGEVDQVIADLIKRIYLLRSQAEDGE--- 209

T IS GEQW KMR V+ I+ PK + G+ + +L+ ++ ++E

Sbjct: 2 TVAISPYGEQWKKMRKVITTEIMSPKRLNWLLGKRTEEADNLVAYVHNMCQKSETNNKHG 61 SEQ ID

NO:15

Query: 210 TVTNVNDLFFKYSMEGVATILYESR-LG----CLENSIP-QLTVEYIEALELMFSMFKTS 263

V +V D+ Y V +++ R G ++ P E+++A+

Sbjct: 62 AVIDVRDVVRHYCHNVVMRMMFGRRHFGKGTZFSDDGGPGPEEKEHMDAIFTALDCLYAF 121

Query: 264 MYAGAIPRWLR 274

+ IPRWLR

Sbjct: 122 CVSDYIPRWLR 132

#### FIG. 13a

Query: 458 RWLRKGDLD 466

RWLR DLD

Sbjct: 129 RWLRGWDLD 137 SEQ ID NO:16

FIG. 13b